REMARKS/ARGUMENTS

Claims 1 and 3-26 remain in this application.

The subject matter of claim 2 has been added to claim 1. Claim 2 has accordingly been cancelled.

Reconsideration is respectfully requested, for the rejection of the claims as unpatentable over the combination of references proposed on page 2 of the Official Action.

Reliance on the reference to Krotzer et al. (hereinafter Krotzer) is believed to be misplaced.

The Official Action suggests that Krotzer teaches the use of creatine and phosphorus for body building in which the daily intake amount may be obtained by a single serving or by multiple serving, and that the most preferred serving for phosphorus is 2,690 mg. Applicant disagrees.

Krotzer describes a composition for human consumption having a nutritionally beneficial substituent (A) and a substituent (B) that stimulates traditional psychological feedback (see claim 1 and para's 0011 and 0014).

Substituent A may be selected from the components described in Table A (page 4) and may be for example potassium. Substituent B may be selected from the list of components described in Table B (page 4 and 5), and may be for example fruit juice or milk.

However, a person skilled in the art will not interpret the amounts given by Krotzer as realistic, since they may be toxic or even lethal.

In particular, on the upper end of the ranges for potassium, Krotzer suggest to ingest a maximum of 27,640 mg potassium, or more preferably 9770 mg potassium. However, the lowest lethal dose of potassium (in the form of potassium chloride) reported for man is 20 mg KCl/kg body weight and for woman 60 mg KCl per kg body weight (corresponding with about 700 mg per dose for a man and 2200 mg potassium for woman.

Case reports have described suicide attempts by a 17 year-old man who ingested 20-30 Klor-Con tablets (each tablet containing 750 mg KCl). The amount ingested by the 17-year old man is equivalent to about 9750 mg potassium. Decontamination (removal of the unabsorbed tablets) by whole bowel irrigation was effective (Su et al., J Toxicol Clin Toxicol 2001; 39(6):641-8). Additionally, Wetli et al. (J. Am. Med. Assoc; 240; 1339) has described in 1978 that "Physicians should be aware that unintentional misuses or abuse of potassium chloride, even in patents with normal renal and cardiac function, may lead to spurious hyperkalemia and death".

A person skilled in the art would immediately conclude that the suggested amounts in Table A cannot refer to the amount of the individual elements. He may conclude that, instead,

Krotzer meant to describe the weight of the complete salt (anion + cation) to be ingested per day. Hence, the weights of the minerals as suggested by Krotzer would be read by the skilled reader as the weights of the complete salts to be ingested.

Table 1 (below) gives the amounts of mineral as percentages of the recommended daily allowances (RDA, National Academy of Sciences, 1998) of the minerals suggested by Krotzer. From this calculation it is clear that the amounts suggested by Krotzer are random and unsubstantiated. The suggested ranges vary between about 1% of the RDA and 16 times (!) the RDA. Also the most preferred ranges for minerals are significantly above the RDA (e.g. 10 times the RDA), while others are near RDA. However, when corrected to the amounts of the completed salts, indeed the suggested ingestion for the most preferred ranges are in conformity with general practice (see Table 2).

TABLE 1: Erroneously described mineral intake by Krotzer as % of RDA

		Ranges of Krotzer		
Mineral	RDA	**Maximum**	**More preferred**	**Most preferred**
Chromium	120 mcg *1	3-16500%	43-3000%	900%
Potassium	2000 mg	1-790%	2-280%	115%
Phosphorus	700 mg	2-2500%	23-980%	269%
Magnesium	400 mg *2	3-1360%	27-490%	125%

*1 between 50 and 200 mcg; generally 120 mcg; *2 420 mg for adult males; 320 mg for adult females

TABLE 2: Corrected daily mineral intake by Krotzer as % RDA

Element	**Most preferred weight (Table A, Krotzer)**	**Salt commonly used**	**Amount of the element**	**%RDA**
Chromium	1100 mcg *1	chromium picolinate (MW = 418.3)	136.7 mcg Cr	114%*
Potassium	2300 mg	potassium chloride (MW = 74.5)	1207 mg K	60%
Phosphorus	2690 mg	potassium phosphate (MW = 173.2	481 mg P	68%
Magnesium	498 mg	magnesium chloride (MW = 59.8)	202 mg Mg	51%

* The high amount of chromium can be explained from the fact that chromium picolinate supplementation has been described to increase lean body mass of football players and young men enrolled in a weight training class. [Evans (1989) The effect of chromium picolinate on insulin controlled parameters in humans Int J Bios Med Research 11:163-180.]

Thus a person skilled in the art would immediately see from the amounts suggested by Krotzer that these amounts do not refer to the amounts of the individual elements, but rather refer to the weight of the complete salt because:

- Krotzer would otherwise suggest potentially lethal amounts of potassium
- Krotzer would suggest amounts for which insufficient toxicological data exist;

- Krotzer would suggest amounts which heavily fluctuate when compared to RDA, without statement, indication or reason to deviate from conventional practice.

Hence, the skilled reader will derive from Krotzer that 2690 mg potassium phosphate, or another phosphate salt, can be used per day. This amount corresponds to about 68% of the daily recommended dosage of phosphorus (see Table 2, above). Applicants' invention concerns the administration of at least 75% of the daily dosage of phosphorus per serving.

The Official Action also indicates that Krotzer teaches the use of creatine and phosphorus for body building. Applicant respectfully disagrees.

Nowhere in the documentation is it suggested to combine creatine and phosphorus: The document does not suggest to combine the nutritionally beneficial substituents creatine and phosphorus (both in Table A). Moreover, phosphorus is not suggested as a preferred nutritional beneficial substituent. If one of ordinary skill were to select one or more substituents from the preferred nutritional beneficial substitutents, he would choose from the preferred substituents [0043, 0044], and not phosphorus.

In conclusion:

- Krotzer does not suggest at least 75% of the RDA of phosphorus per serving

- Krotzer does not suggest a combination of creatine and at least 75% of the RDA of phosphorus per serving.
- Krotzer does not suggest the combination of blood buffer and at least 75% of the RDA of phosphorus per serving.
- Krotzer does not suggest creatine and blood buffer.
- Krotzer does not suggest creatine and blood buffer and at least 75% fo the RDA of phosphorus per serving.

Claims 1-26 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Simone (U.S. 5,397,786) in view of Weinstein et al. (U.S. 6,013,290), WO9604240, Fang (U.S. 5,886,040), Webster's Dictionary (10th edition), Odain et al. (Schaum's Outline), Hultman et al. (U.S. 5,767,159), St Cyr et al. (U.S. 6,159,942) and Krotzer et al. (U.S. 2001/0008641).

Applicant respectfully traverses the above rejection.

The basic requirements of a *prima facie* case of obviousness are laid down in MPEP 2143. To establish a *prima facie* case of obviousness, three basic criteria must be met.

A. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the *Montefiore Hospital*, 732 F.2d at 1577, 221 USPQ 929, 933: Obviousness "cannot be established by combining

the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." In other words, teachings of references can be combined only if there is some suggestion or incentive to do so.

B. There must be reasonable expectation of success, i.e. whether the prior art would also have revealed that in so doing, those of ordinary skill would have a reasonable expectation of success (see In re Dow Chemical Co. 837 F 2d 469, 473, 5 USPQ 2d 1529, 1531). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In *re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

C. The prior art reference (or references when combined) must teach or suggest all the claimed limitations.

Furthermore, when applying 35 U.S.C. §103, the following tenants of patent law must be adhered to (MPEP 2141);

(A) The claimed invention must be considered as a whole;

(B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;

(C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(D) Reasonable expectation of success is the standard by which obviousness is determined.

Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

Suggestion to combine or modify (MPEP 2143.01)

The Official Action indicates that the claimed invention is *prima facie* obvious. It concludes *prima facie* obviousness of the present invention by selecting a variety of references from the state of the art and selecting very specific parts from the cited references. It then substantiates this reasoning by stating that:

"Rather, the test for obviousness is what the combined teachings of the references would have suggested to those of ordinary skill in the art (In re Keller, 642 F2d 413, 208 USPQ 871 (CCPA 1981)."

However, In re Keller does not imply that each and every disclosure may be combined randomly, and that specific parts or paragraphs of different disclosures may be combined

without any reason, i.e. without it being obvious for the skilled person that such combination would be desirable, see

In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) "The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination."; and

ASC Hosp. Sys. Inc vs. Montefiore Hospital, 732 F.2d at 1577, 221 USPQ 929, 933: Obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination."

Hence, the Office Action seems to ignore the requirements that there needs to be some implicit or explicit teaching, suggestion or incentive to combine the references (MPEP 2143.01). At the very least, it omits to provide any reasoning (expressly or impliedly) which indicates why the skilled person would combine the cited references.

There is no reason for the skilled person to combine the cited references, for the following reasons:

In the present case, the cited references lack any explicit teaching, suggestion or incentive to be combined, since (A) the cited references are not in the field of applicants' endeavor and (B) are not reasonably pertinent to the particular

problem with which the Applicant, were concerned (MPEP 2141.01(a)).

(A) The field of endeavor of the cited references are respectively;

Fang: Palatability of creatine preparations

Simone: Rehydration drinks

Weinstein: Administration regimen for beverages before and after exercise sessions

St Cyr: Pentoses for increasing energy levels

Hultman: Method for increasing intracellular creatine depot

Negrisoli: Solubility improvement of creatine.

Krotzer: Compliance with a nutritional by beneficial substituent intake.

From the above, it is clear that several of the cited references relate to a completely different field of endeavor, and therefore, the skilled person would not have combined the cited teachings.

The difference of PTO classification of references cited in the present case provides further evidence of "non-analogy" (MPEP 2141.01(a)). The following are the main classification codes of the cited U.S. patent documents: Fang et al. 514/634; Simone 514/300; Krotzer 424/725; Weinstein 426/74; St Cyr 514/23; Hultman 514/565). Not one of the classes of the

cited references overlaps. Hence, this provides further evidence of the lack of an explicit incentive to combine the cited references.

Absent an explicit incentive, the test for an implicit showing is what the combined teachings, knowledge, of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art. In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). See also In re Fine, 837 F.2d 1071, 5USPQ2d 1596 (Fed. Cir. 1988); In re Jones, 958 F.2d 347,21 USPQ2d 1941 (Fed. Cir. 1992).

The problem solved by Applicants' invention relates to the improvement of performance and anaerobic working capacity by administering creatine and at least 75% of the RDA of phosphorus. Not one of the cited references recognizes or even hints at this problem, particularly since not one of the cited references suggests the use of a combination of creatine and at least 75% of the RDA of phosphorus per serving and problems related thereto. Hence, at least part of the invention lies in the discovery of the source of the problem. A persuasive assertion of the problem is given in the specification.

Applicants found that the effects of at least 75% of the RDA of phosphorus per serving phosphorus and creatine on performance could be further improved. The cited references fail

to provide or suggest the solution to the problem which was found by the Applicant, namely co-administering blood buffer with the creatine and at least 75% of the RDA of phosphorus per serving, wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1. Absent any recognition or suggestion of the problem in the cited references, the solution to the problem cannot be obvious.

Hence, absent any suggestion to combine or modify the cited references, Applicants' invention is not obvious in view of the cited references.

The Official Action further asserts that:

In response to Applicants' argument that is has different reasons for combining creatine, phosphorus and blood buffer, the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

However;

a. The cited references do not provide any reason to be combined to teach the combination of creatine, at least 75% of the RDA of phosphorus per serving and blood buffer wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1 (see above);

b. Even if combined, a combination of creatine at least 75% of the RDA of phosphorus per serving and blood buffer wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1 would not naturally flow from the cited references; and

c. Applicants did not recognize another advantage from of the combination. Because the combination is novel and not suggested, no advantage has been recognized from the present combination. Hence, the present case lacks analogy with Ex parte Obiaya, 227 USPQ 58, 60 (Bd. Pat. App. & Inter 1985).

The Official Action further asserts that:

"the prior art teaches that carbohydrates, buffers and phosphorus are necessary supplements for persons who are exercising to replenish energy stores and counteract increased blood acidity."

Applicants' invention however relates to a combination of creatine, at least 75% of the RDA of phosphorus per serving and blood buffer wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1.

Hence absent any implicit or explicit suggestion to combine the cited references, the cited references may only be

found with the benefit of hindsight, which is impermissible (MPEP 2141).

Moreover, the cited references do not teach, suggest, or contain an incentive for the skilled person to pick and choose and combine specific elements of the cited references. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).

Reasonable expectation of success (MPEP 2141 and 2143)

As described in the specification, Applicants' invention was born from the finding that creatine and high phosphorus can increase the glycolytic capacity of the cells and thereby improve body performance; however, that increase of glycolytic capacity (and thus improvement of body performance) by coadministration of creatine and high phosphorus is bound to an upper level. This is not suggested in any of the cited references.

With this recognition, it was surprisingly found that blood buffer could remove the inhibitory effects of creatine and high phosphorus with a weight ratio of phosphorus to creatine of about 1:25 to about 10:1.

The cited references do not suggest a combination of creatine and at least 75% of the RDA of phosphorus. Furthermore,

the cited references do not suggest that such a problem exists. Hence, from the combined teaching of the cited references, one of ordinary skill would not even be motivated to solve the problem, i.e. to arrive at Applicants' invention. Furthermore, in the absent of any recognition of the problem, the person of ordinary skill would not foresee or predict that the combination of creatine, at least 75% of the RDA of phosphorus and blood buffer wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1 would be advantageous for the improvement of anaerobic working capacity.

Not one of the cited references reveals any beneficial effect of phosphorus. Simone only describes that the salts of a metal of the groups I and II of the Periodic System are advantageously incorporated. Simone does not disclose or give any hint of the advantageous effects of including a particular anionic group in the electrolyte salt composition, nor does Simone give any hint as to the improvements that can be expected from choosing phosphorus-containing salts. Hence, the skilled artisan would not suspect from Simone that the inclusion of phosphorus in an amount of at least 75% of the daily recommended intake would have an advantageous effect.

Also, Weinstein et al. does not disclose the beneficial effects of phosphorus. Weinstein et al. mentions that phosphates if they are to be found to have a beneficial effect, may be

included in the composition described. This is however no indication that phosphate has any beneficial effects.

Krotzer describes that a daily amount of 68% of the RDA of phosphorus may be administered, but does not give any reason for the inclusion of phosphorus, nor does Krotzer describe phosphorus as a preferred substituent. Krotzer describes other constituents as being preferred constitutents, and thereby even teaches away from Applicants' invention. St Cyr et al. does not suggest the administration of phosphorus. Fang does not suggest the administration of phosphorus. Negrisoli et al. do not suggest the administration of phosphorus.

Absent any indication or reason in the cited references to include phosphorus in a composition suitable for oral administration and aimed to improve performance, one of ordinary skill would not intentionally include phosphorus in such a composition, let alone include at least 75% of the RDA of phosphorus per serving based on the cited references. Still, there may be some minor amounts of phosphorus included in the composition, through the inclusion of salts as described by Simone, as described in the earlier reply; if so, these amounts will be far below the at least 75% of the RDA per serving. Simone furthermore explicitly teaches an upper level of the salts to be included and hence, teaches away from the present invention.

Hence, absent any recognition of the importance of phosphorus in a composition for improving performance, the combined teachings of the cited references would not suggest to those of ordinary skill in a composition suitable for improving performance, containing at least 75% of the RDA of phosphorus, creatine and blood buffer.

All claim limitations must be suggested (MPEP 2143)

The Official Action asserts that:

"... as suggested by Krotzer, amounts falling within the scope of the claimed amounts are preferred for the purpose of bodybuilding"

As explained above, Krotzer does not teach the use of 2690 mg phosphorus per serving, but instead describes the inclusion of 68% of the RDA (481 mg) of the phosphorus per day. The other ranges suggested by Krotzer would not be considered by skilled persons, since they include lethal dosages.

The prior art reference (or references when combined) must teach or suggest all the claimed limitations (MPEP 2143). However:

1. Not one of the cited references suggest to include at least 75% of the RDA of phosphorus in a serving or suggests the beneficial effects of phosphorus.

2. Not one of the cited references suggests a composition containing creatine and at least 75% of the RDA of phosphorus in a serving wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1.

3. The present invention is limited to a combination of creatine, at least 75% of the RDA of phosphorus and blood buffer wherein the weight ratio of phosphorus to creatine is about 1:25 to about 10:1. Nowhere in the cited references it is suggested to combine these components.

Hence, since not all claim limitations are suggested in the cited references, Applicants' invention is not prima facie obvious.

Anaerobic working capacity and St. Cyr et al.

The Official Action also asserts that:

"... the prior art teaches that creatine and phosphate are used in an anaerobic process to replenish ATP, which is the cellular source of energy (St. Cyr. et al.). As such, one of ordinary skill in the art would expect that anaerobic working capacity would be increased."

In column 1, lines 29-43 and 60-64, St. Cyr et al. describe the energy metabolism of the cell. The mere discussion of an intracellular metabolic pathway does however not provide

one of ordinary skill any indication as to what components can be orally administered beneficially for improving body performance. Many hurdles have to be overcome, such as bioavailability of the orally administered component, potential toxicity, potential side effects, effectiveness of precursor etc. For example, according to Op 't Eijnde, B et al (2001), oral ribose (a precursor of ATP) supplementation with 4-g doses four times a day does not beneficially impact on postexercise mustle ATP recovery and maximal intermittent exercise performance. (Op 't Eijnde, et al. J Appl. Phys (2001) Vol. 91, No. 5, pp. 2275-2281).

Furthermore, if the supplementation of phosphorus were evident from discussion of the intracellular pathways (which have been known for decades), St Cyr would have suggested the use of phosphorus, St. Cyr lacks any suggestion to administer phosphorus.

A further indication of unobviousness of the present invention is unexpected results. The extent of improvement of the anaerobic working capacity in humans (almost 50%!!!) as described in Example 1 of the specification was unexpected for one of ordinary skill, being aware of the state of the art including the cited references. The presence of an unexpected result is an indication for non-obviousness. The extent of improvement would be a surprise for one of ordinary skill, and should be regarded as an indication for unobviousness.

The Official Action also gives no reasons for obviousness of claim 4 (i.e. wherein the composition contains a creatine salt); claim 5 (wherein the creatine is highly hydrosoluble); claim 6 (wherein the creatine is an organic creatine salt); claim 7 (wherein the creatine has a solubility above 6 grams/100 ml water); claim 8 (wherein the creatine salt comprises an anionic component selected from the group consisting of carbonate, biocarbonate, citrate and citric acid); claim 12 (wherein the composition further comprises a carbohydrate); claim 15 (wherein the composition further comprises a carbohydrate; claim 15 (wherein the composition further comprises a pentose) and claim 17 (wherein the composition further comprises a sodium salt).

Therefore, it is evident that these dependent claims are also patentable, not only for their dependency from allowable base claims, but also by virtue of the further features of novelty that they separately recite.

In view of the present amendment and the foregoing remarks, therefore, it is believed that this application has been placed in condition for allowance, and reconsideration and allowance are respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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RJP/psf